5-14-02

GP1637

Case 4584

#5/Election

5/21/02

Serial No. 09/942,342

CERTIFICATION OF MAILING

CERTIFICATION UNDER 37 CFR 1.10

Express Mail Number: EL 897626083 US Date of Deposit: May 10, 2002

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor: Ewing Attorney Docket No. 4584

Serial No: 09/942,342 Art Unit: 1637

Filed: August 27, 2001 Examiner: J. Riley

Title: NON-FLUORESCENT QUENCHER COMPOUNDS AND BIOMOLECULAR ASSAY

RESPONSE TO RESTRICTION REQUIREMENT UNDER 37 CFR § 1.111

Assistant Commissioner for Patents
Washington, D. C. 20231

Sir:

With reference to the Office communication mailed April 30, 2002, reconsideration of the application is respectfully requested. Claims 1-75 are pending. In the Office communication mailed April 30, 2002, the claims were divided into nine groups. The restriction is respectfully traversed. Applicant provisionally elects claim group I, claims 1-25, solely to comply with 37 CFR 1.143.

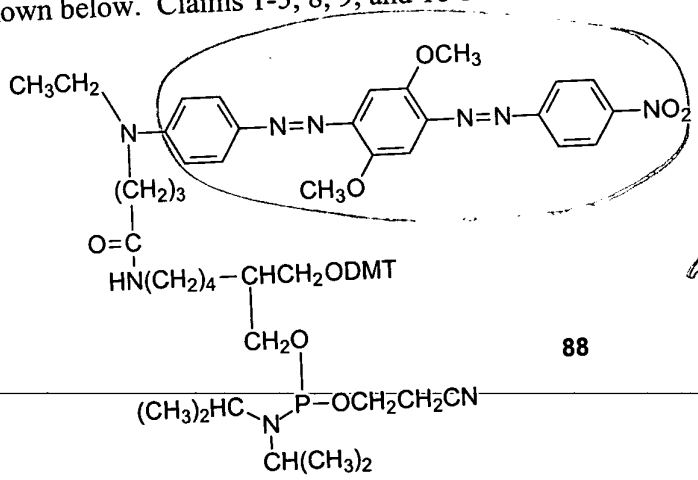
It is noted that Groups II, III, and VI are all composition claims. The Examiner has classified them in the same class 536 and the same subclass 26.6. The Examiner has not provided sufficient substantive basis justifying the restriction of these composition claims. In particular, the Examiner has provided no explanation as to how these claim sets are both independent and distinct.

It is further noted that Groups IV, V, VII, VIII, and IX are all method claims. The Examiner has classified them in the same class 435. Groups V, VIII, and IX are classified in the same

subclass 6. The Examiner has not provided sufficient substantive basis justifying the restriction of these method claims. In particular, the Examiner has provided no explanation as to how these claim sets are both independent and distinct.

Accordingly, the restriction requirement appears to be improper. The applicant maintains that restriction into nine inventions is unduly burdensome and unjustified under 35 USC 121. Reconsideration is respectfully requested.

In response to the requirement for an election of species under 35 USC § 121, applicant provisionally elects the species of compound **88**, found at page 57, Example 44 of the specification, and shown below. Claims 1-5, 8, 9, and 18-20 read on the elected species.



88

9 is not disclosed in claim? not apparent

Applicants expressly reserve the right to prosecute claims drawn to the unelected claims and unclaimed subject matter in one or more timely filed continuation, divisional and/or continuation-in-part applications.

PETITION FOR TIME EXTENSION and FEE AUTHORIZATION

This reply is considered timely filed. If any time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from deposit account number **01-2213**.

Respectfully submitted,

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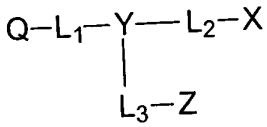
Appendix:

1. A fluorescence quencher composition having the structure:



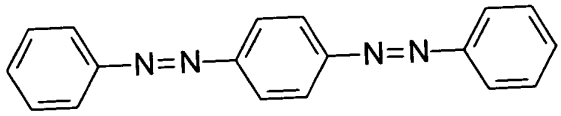
wherein Y is selected from N and CR, where R is H, C_1–C_6 alkyl or C_5–C_{14} aryl;

L_1, L_2, and L_3 are independently selected from a bond, C_1–C_{12} alkyldiyl, C_1–C_{12} alkoxyldiyl, C_1–C_{12} alkylaminodiyl, C_1–C_{12} alkylamidediyl, C_5–C_{14} aryldiyl, and 1-20 ethyleneoxy units;

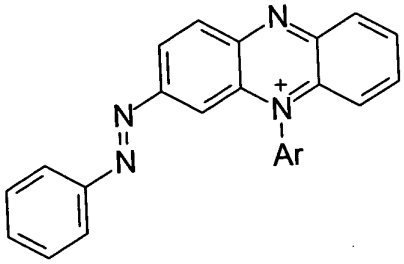
X is an amino acid, a polypeptide, a nucleoside, a nucleotide, a polynucleotide, or a protected form thereof; or X is an acid-labile protecting group;

Z is selected from H, CO_2H, OH, NH_2, NHR, NR_2, SH, an ester, a cleavable linker, a solid support, a reactive linking group, and a label selected from a fluorescent dye, a hybridization-stabilizing moiety, a chemiluminescent dye, and an affinity ligand; and

Q is selected from the diazo structures:



and



wherein Ar is C_5–C_{14} aryl; one of the aryl carbons of the diazo structures is the site of attachment to L_1; at least one aryl carbon of each diazo structure is substituted with an electron-withdrawing group and at least one aryl carbon of each diazo structure is substituted with an electron-donating group.

2. The fluorescence quencher composition of claim 1 wherein the electron-withdrawing groups are selected from NO_2, CN, CF_3, CO_2H, CO_2R, $C(O)NH_2$, C(O)NHR, $C(O)NR_2$, CHO, C(O)R, SO_2R, SO_2CF_3, SO_2OR, SO_3H, NO, and C_5–C_{14} aryl, where R is H, C_1–C_{12} alkyl or C_5–C_{14} aryl.

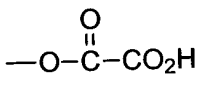
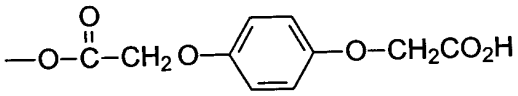
3. The fluorescence quencher composition of claim 2 wherein a NO_2 is *para* to a diazo group.

4. The fluorescence quencher composition of claim 1 wherein the electron-donating groups are selected from O^-, S^-, NR_2, NHR, NH_2, NHC(O)R, OR, OH, OC(O)R, SR, SH, Br, I, Cl, F, R, and C_5–C_{14} aryl, where R is H, C_1–C_{12} alkyl or C_5–C_{14} aryl.

5. The fluorescence quencher composition of claim 4 wherein a OCH_3 is *ortho* or *meta* to a diazo group.

6. The fluorescence quencher composition of claim 1 where Z is OH

7. The fluorescence quencher composition of claim 1 where Z is an ester selected from the structures:


,

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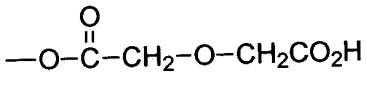
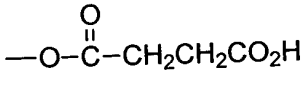

, and

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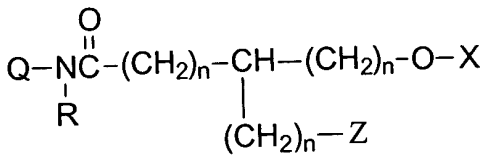
8. The fluorescence quencher composition of claim 1 selected from the structures:



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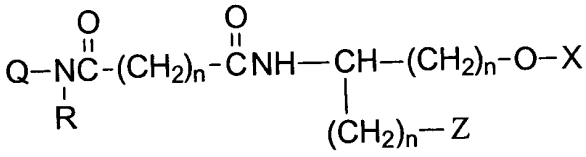
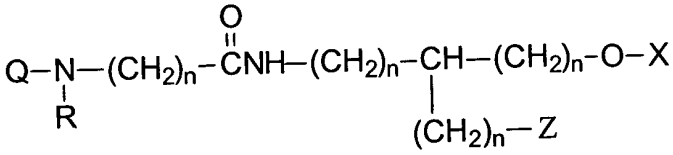


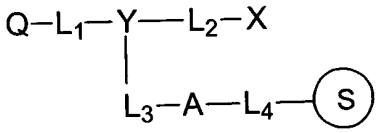
, and



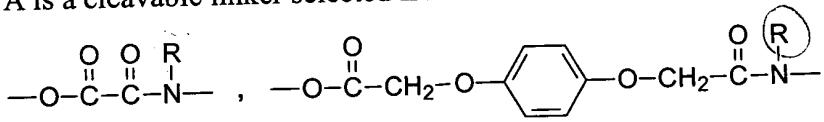
where n is 1 to 12.

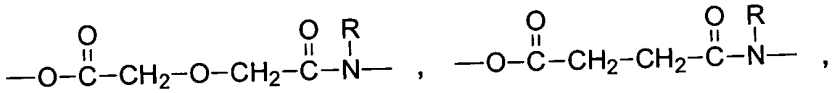
9. The fluorescence quencher composition of claim 1 wherein X is selected from DMT, MMT, trityl, substituted trityl, pixyl, and trialkylsilyl.

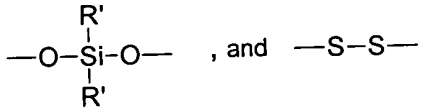
10. The fluorescence quencher composition of claim 1 having the structure:



wherein A is a cleavable linker selected from the structures:







, and

where R' is H, C_1–C_{12} alkyl or C_1–C_{12} alkoxy;

L_4 is selected from a bond, C_1–C_{12} alkyldiyl, C_1–C_{12} alkoxyldiyl, C_1–C_{12} alkylaminodiyl, C_1–C_{12} alkylamidediyl, C_5–C_{14} aryldiyl, and 1-20 ethyleneoxy units; and

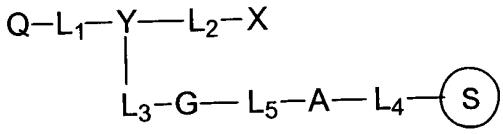
(S) is a solid support.

11. The fluorescence quencher composition of claim 10 wherein X is a nucleotide.

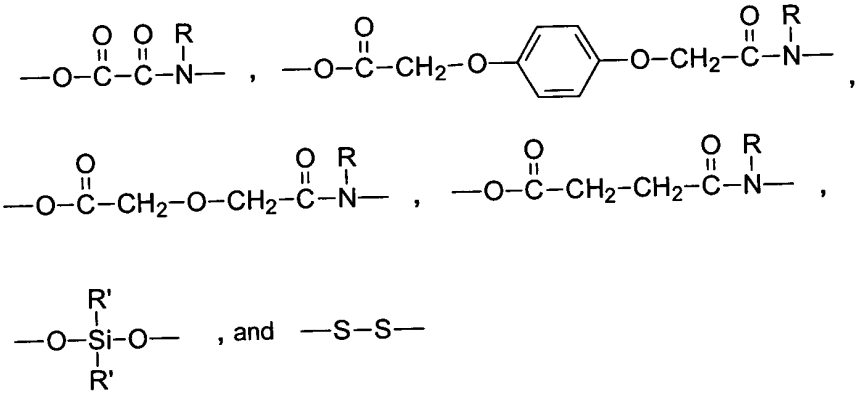
12. The fluorescence quencher composition of claim 10 wherein the solid support is selected from polystyrene, controlled-pore-glass, silica gel, silica, polyacrylamide, polyacrylate, hydroxyethylmethacrylate, polyamide, polyethylene, polyethyleneoxy, and copolymers and grafts of such.

13. The fluorescence quencher composition of claim 10 wherein the form of the solid support is selected from a particle, a bead, a membrane, a frit, a fiber, a tube, a capillary, a slide, a plate, a micromachined chip, an alkanethiol-gold layer, a magnetic bead, a non-porous surface, an addressable array, and polynucleotide-immobilizing medium.

14. The fluorescence quencher composition of claim 1 having the structure:



wherein A is a cleavable linker selected from the structures:



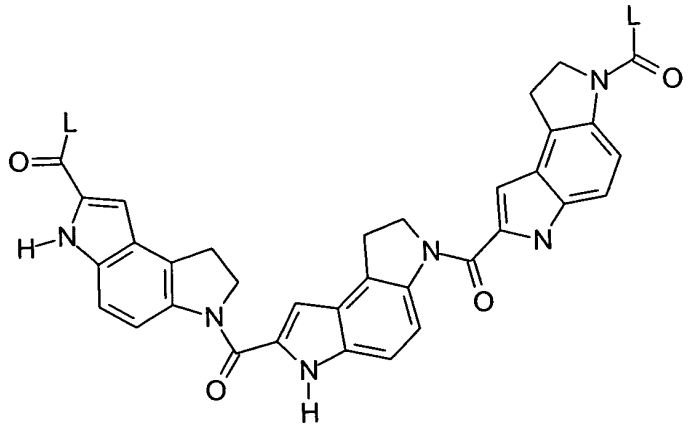
where R is H, C_1–C_{12} alkyl or C_1–C_{12} alkoxy;

L_4 and L_5 are independently selected from a bond, C_1–C_{12} alkyldiyl, C_1–C_{12} alkoxyldiyl, C_1–C_{12} alkylaminodiyl, C_1–C_{12} alkylamidediyl, C_5–C_{14} aryldiyl, and 1-20 ethyleneoxy units;

G is a hybridization-stabilizing moiety; and

(S) is a solid support.

15. The fluorescence quencher composition of claim 14 in which G comprises:

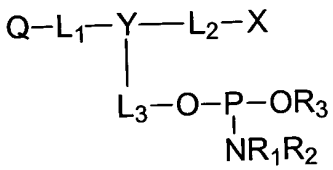


where L are the sites of attachment to L_3 and L_5.

16. The fluorescence quencher composition of claim 14 wherein the solid support is selected from polystyrene, controlled-pore-glass, silica gel, silica, polyacrylamide, magnetic beads, polyacrylate, hydroxyethylmethacrylate, polyamide, polyethylene, polyethyleneoxy, and copolymers and grafts of such.

17. The fluorescence quencher composition of claim 14 wherein the form of the solid support is selected from a particle, a bead, a membrane, a frit, a fiber, a tube, a capillary, a slide, a plate, a micromachined chip, an alkanethiol-gold layer, a magnetic bead, a non-porous surface, an addressable array, and polynucleotide-immobilizing medium.

18. The fluorescence quencher composition of claim 1 having the structure:

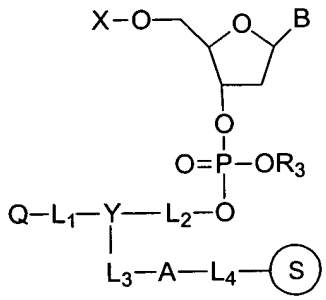


wherein X is an acid-labile protecting group; R_1 and R_2 are individually selected from isopropyl, morpholino, methyl, ethyl and C_5–C_{14} aryl; R_1 and R_2 taken together are C_4–C_{11} cycloalkyl or morpholino; and R_3 is C_1–C_6 alkyl or C_5–C_{14} aryl.

19. The fluorescence quencher composition of claim 18 wherein R_1 and R_2 are each isopropyl and R_3 is cyanoethyl.

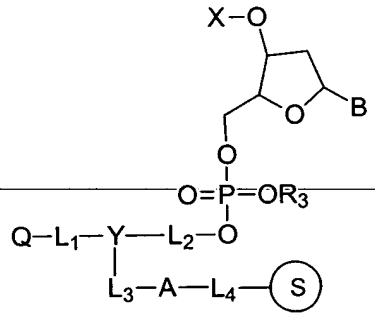
20. The fluorescence quencher composition of claim 18 wherein X is selected from DMT, MMT, trityl, substituted trityl, pixyl, and trialkylsilyl.

21. The fluorescence quencher composition of claim 11 having the structure:



wherein X is an acid-labile protecting group; B is a nucleobase; and R_3 is selected from H, C_1–C_6 alkyl, and C_5–C_{14} aryl.

22. The fluorescence quencher composition of claim 11 having the structure:



wherein X is an acid-labile protecting group; B is a nucleobase; and R_3 is selected from H, C_1–C_6 alkyl, and C_5–C_{14} aryl.

23. The fluorescence quencher composition of claim 1 where X is a polynucleotide.

24. The fluorescence quencher composition of claim 23 wherein the polynucleotide comprises one or more N-[2-(aminoethyl)]glycine units having a nucleobase attached to nitrogen through a methylene carbonyl linkage.

25. The fluorescence quencher composition of claim 23 wherein the polynucleotide comprises one or more 2'-4' or 3'-4' bicyclic sugar modifications.